REMARKS

Claim 1 has been amended simply for clarification in response to the rejection under 35 U.S.C. § 112, paragraph two. Applicants believe that the claim was already clear in that it indicated that the chemically defined components were the only sources of carbon and nitrogen for the growth of the organism. The confusion evinced by the Office is not completely understood. In reviewing the rejection, it appears that an additional element, which was never in the claims, is envisioned by the Office - *i.e.*, that a mutant strain is the nature of the microbial strain in the claims. That has never been a claim limitation. In any event, it is believed that the amendment clarifies that the chemically defined components are the only sources of carbon and nitrogen in this industrial scale production. Though made after final, entry of the amendment is requested, as there was no way this amendment could have been made previously.

The Rejection Under 35 U.S.C. § 103

All pending claims were rejected as assertedly obvious over Hogye, *et al.*, in view of Bovenberg, *et al.*, and, now, the addition of "Microbiology" pages 853-856.

It is first noted that the "Microbiology" document is the only document which even considers in any way the essential claim limitation that the volume scale be at least 10 m^3. Absent this document, there is no basis for the suggestion of this claim limitation at all.

Respectfully, it is believed that the Office has mischaracterized the teachings of the "Microbiology" document. The Office points to pages 855-856 as disclosing a "similar standard chemically defined medium" as that claimed.

Applicants are unable to find such a disclosure. There is nothing on these pages which describes any kind of chemically defined medium where chemically defined materials are used

as carbon and nitrogen sources. The step 5 pointed to by the Office is explicitly excluded by the limitation that the medium contains no complex raw materials. As is clear from the specification, the industrial processes claimed in this application are for *de novo* production of β-lactams, not simply the conversion of a complex raw material precursor of the β-lactam into the β-lactam *per se*. It is this conversion that item 5 on page 855 describes.

In point of fact, the "Microbiology" document is completely irrelevant to the present invention - it merely shows that penicillin was produced on an industrial scale; it is completely silent with regard to the use of chemically defined medium as required by the present claims.

If anything, the "Microbiology" document suggests media that are not chemically defined. For example, note Figure 40-4 on page 856 which describes the manufacture of penicillin using a medium of corn steep liquor, lactose salts and other ingredients. The use of corn steep liquor, a very complex raw material, would certainly preclude this medium from being chemically defined.

Applicants enclose as Exhibit B several pages from the "Traders' Guide to Fermentation Media Formulation" a publication which represents the understanding of the art. In the relevant portion of this publication, the distinction between chemically defined media and complex or natural media is set forth. As stated on page 2,

> Often a culture medium is prepared using pure compounds in precisely defined proportions. Media of this type are called synthetic or defined and examples are shown in Table 1. Alternatively, media can be formulated using ingredients of natural origin which are not completely defined chemically such as blood, meat extracts, molasses and cotton seed flour. These are referred to as complex or natural media...

It should thus be apparent that media, such as those described in "Microbiology" on page 856, are not included within the scope of the claims, and there is no suggestion in "Microbiology" that defined media should be used in industrial scale processes.

Reverting, now, to the question of the use of compounds as precursors, the understanding in the art is that precursors for penicillins are only such compounds as phenylacetic acid (penicillin G) or phenoxyacetic acid (penicillin V). Clearly carbohydrates are not considered precursors, nor are nitrogen salts - see, for example, claim 4.

Hogye and Bovenberg are irrelevant. Hogye, as pointed out in the previous response, is silent on the volume of the culture. It is acknowledged in the specification repeatedly, for example, on page 3, lines 8-18, that defined media to produce materials on a laboratory scale is well known. The problem arises when defined media are to be used industrially. There is no indication in Hogye that industrial scale production is described or contemplated. (It is also not entirely clear that ammonium sulfate and ammonium hydroxide are actually the sole sources of nitrogen.)

Bovenberg, similarly, describes only small scale production of phenylacetyl-7-ADCA, and not even on chemically defined medium. Rather, it describes the conversion of phenylacetyl-7-ADCA using phenylacetic acid as a precursor; the point of Bovenberg is to utilize a modified organism which contains the expandase gene.

Whatever motivation there might be to combine Bovenberg with Hogye is unclear. The Office says that the process of Hogye to include Bovenberg's process for the beneficial purpose of producing the claimed invention's process of production of penicillin V and/or adipoyl-7-ADCA does not address the point of the invention which is the use of chemically defined medium on an industrial scale. Even if Bovenberg and Hogye are combined, the

invention does not result since both documents describe fermentations only on a research scale and, to the extent chemically defined media are used in that context, this is acknowledged practice. The invention lies in the extension of the use of chemically defined media to an industrial scale, a matter on which both Hogye and Bovenberg are completely silent.

As to any motivation for combining the teachings of Bovenberg and Hogye with the "Microbiology" document, there is none even proposed by the Office. There appears to be no visible connection between these documents other than their discussion of β-lactams. And even if these documents are combined, there is no teaching that any chemically defined media as disclosed in, for example, Hogye would be useful in the industrial processes described by "Microbiology."

In summary, the basis for rejection appears to be that because the use of chemically defined media on a research scale is known and because industrial production of β-lactams is known, it would be obvious to utilize chemically defined media in industrial scale processes.

Respectfully, the reason that this basis for rejection is in error is that no suggestion has been found in the art to utilize chemically defined media for the production of fermentation products, including β-lactams, on an industrial scale. That suggestion is found only in the present specification. If the Office is able to point to a suggestion for this combination in the art, applicants respectfully request that such suggestion be brought to their attention so that they might properly respond. It is well established that when claims are rejected over a combination of documents, some suggestion to make the combination must be found in the art itself, not solely in applicant's own disclosure. See, for example, *In re Dembiczak*, 175 F3d 994, 50 USPQ2d 1614 (Fed. Cir. 1999); *W.L. Gore & Associates v. Garlock, Inc.*, 721 F2d 1540,

220 USPQ 303 (Fed. Cir. 1983); and *In re Fritch*, 972 F2d 1260, 23 USPQ2d 1780 (Fed. Cir. 1992) to name a few.

Accordingly, applicants believe that the sole outstanding basis for rejection of the pending claims may properly be withdrawn.

CONCLUSION

A simple amendment is proposed for clarification of claim 1 so as to overcome the rejection under 35 U.S.C. § 112, paragraph two. As there is no showing of any suggestion in the art that chemically defined medium could be used to prepare β-lactams on an industrial scale, the invention as claimed is not rendered obvious by the art, and applicants respectfully request that the pending claims be passed to issue forthwith.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 246152012710.

Respectfully submitted,

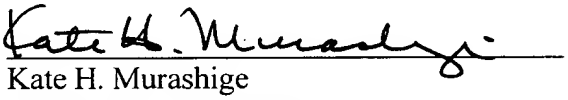
Dated: December 27, 2002 By: 

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EXHIBIT A. - VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

1. (Thrice amended) A process for the production of a β-lactam, comprising the steps of:

a) fermenting on a volume scale of at least 10 m^3, a microbial strain that produces a β-lactam in a fermentation medium which [utilizes] contains only chemically defined components as carbon and nitrogen sources and contains no complex raw materials, and

b) recovering the β-lactam from the fermentation medium.